Docket No.: Serial No..

AREN-0315

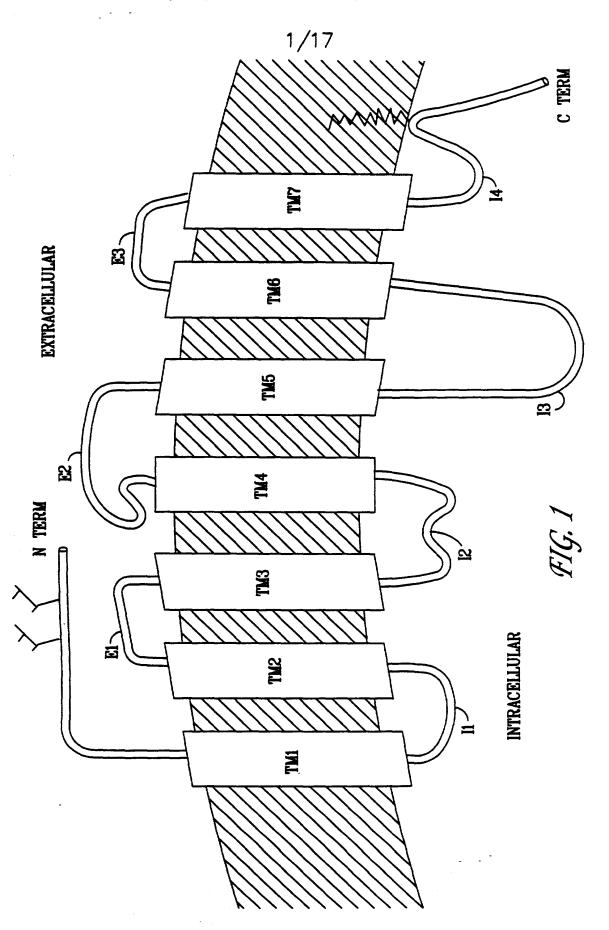
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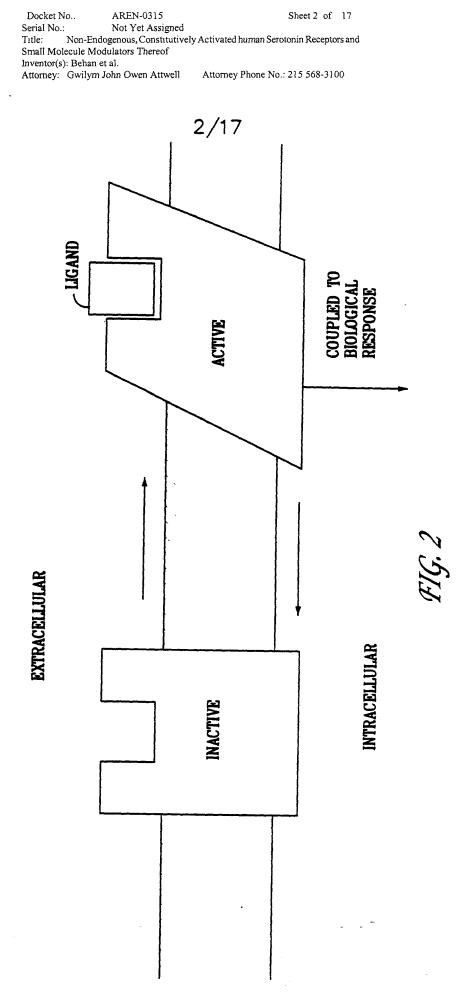
Serial No.. Not Yet Assigned
Title: Non-Endogenous, Constitutively Activated human Serotonin Receptors and

Small Molecule Modulators Thereof

Inventor(s): Behan et al. Attorney: Gwilym John Owen Attwell

Attorney Phone No.: 215 568-3100





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Non-Endogenous, Constitutively Activated human Serotonin Receptors and Title.

Small Molecule Modulators Thereof

lnventor(s). Behan et al

Attorney: Gwilym John Owen Attwell Attorney Phone No.: 215 568-3100

ATGGATATTCTTTGTGAAGAAAATACTTCTTTGAGCTCAACTACGAACTCCCTAATGCAATTA **AATGATGACAACAGGCTCTACAGTAATGACTTTAACTCCGGAGAAGCTAACACTTCTGATGCA** TTTAACTGGACAGTCGACTCTGAAAATCGAACCAACCTTTCCTGTGAAGGGTGCCTCTCACCG TCGTGTCTCTCCTTACTTCATCTCCAGGAAAAAAACTGGTCTGCTTTACTGACAGCCGTAGTGA TTATTCTAACTATTGCTGGAAACATACTCGTCATCATGGCAGTGTCCCTAGAGAAAAAGCTGC AGAATGCCACCAACTATTTCCTGATGTCACTTGCCATAGCTGATATGCTGCTGGGTTTCCTTGT CATGCCCGTGTCCATGTTAACCATCCTGTATGGGTACCGGTGGCCTCTGCCGAGCAAGCTTTGT GCAGTCTGGATTTACCTGGACGTGCTCTTCTCCACGGCCTCCATCATGCACCTCTGCGCCATCT CGCTGGACCGCTACGTCGCCATCCAGAATCCCATCCACCACAGCCGCTTCAACTCCAGAACTA AGGC ATTTCTG AAAATCATTGCTGTTTGGACCATATCAGTAGGTATATCCATGCCAATACCAG TCTTTGGGCTACAGGACGATTCGAAGGTCTTTAAGGAGGGGAGTTGCTTACTCGCCGATGATA **ACTITGTCCTGATCGGCTCTTTTGTGTCATTTTTCATTCCCTTAACCATCATGGTGATCACCTAC** TTTCTAACTATCAAGTCACTCCAGAAAGAAGCTACTTTGTGTGTAAGTGATCTTTGGCACACGG GCCAAATTAGCTTCTTTCAGCTTCCTCCCTCAGAGTTCTTTGTCTTCAGAAAAGCTCTTCCAGC GGTCGATCCATAGGGAGCCAGGGTCCTACACAGGCAGGAGGACTATGCAGTCCATCAGCAAT GAGCAAAAGGCATGCAAGGTGCTGGGCATCGTCTTCTTCCTGTTTGTGGTGATGTGGTGCCCCT TTCTTCATCACAAACATCATGGCCGTCATCTGCAAAGAGTCCTGCAATGAGGATGTCATTGGG CACTGTTCAACAGACCTATAGGTCAGCCTTTTCACGGTATATTCAGTGTCAGTACAAGGAAA <u>ACAAAAACCATTGCAGTTAATTTTAGTGAACACAATACCGGCTTTGGCCTACAAGTCTAGCC</u> AACTTCAAATGGGACAAAAAAAGAATTCAAAGCAAGATGCCAAGACAACAGATAATGACTGC TCAATGGTTGCTCTAGGAAAGCAGTATTCTGAAGAGGCTTCTAAAGACAATAGCGACGGAGT GAATGAAAAGGTGAGCTGTGTGA

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Non-Endogenous, Constitutively Activated human Serotonin Receptors and Small Molecule Modulators Thereof

Inventor(s): Behan et al.

Attorney: Gwilym John Owen Attwell Attorney Phone No.: 215 568-3100

FIG. 3B

MDILCEENTSLSSTTNSLMQLNDDNRLYSNDFNSGEANTSDAFNWTVDSENRTNLSCEGCLSPSCL SLLHLQEKNWSALLTAVVIILTIAGNILVIMAVSLEKKLQNATNYFLMSLAIADMILGFLVMPVSM LTILYGYRWPLPSKLCAVWIYLDVLFSTASIMHLCAISLDRYVAIQNPIHHSRFNSRTKAFLKIIAVW TISVGISMPIPVFGLQDDSKVFKEGSCLLADDNFVLIGSFVSFFIPLTIMVITYFLTIKSLQKEATLCVS DLGTRAKLASFSFLPQSSLSSEKLFQRSIHREPGSYTGRRTMQSISNEQKACKVLGIVFFLFVVMWC PFFTTNIMAVICKESCNEDVIGALLNVFVWIGYLSSAVNPLVYTLFNKTYRSAFSRYIQCQYKENKK PLQLILVNTIPALAYKSSQLQMGQKKNSKQDAKTTDNDCSMVALGKQYSEEASKDNSDGVNEKV SCV

FIG. 4B

MVNLRNAVHSFLVHLIGLLVWQCDISVSPVAAIVTDIFNTSDGGRFKFPDGVQNWPALSIVIIIIMTIGGN ILVIMAVSMEKKLHNATNYFLMSLAIADMLVGLLVMPLSLLAILYDYVWPLPRYLCPVWISLDVLFSTASI MHLCAISLDRYVAIRNPIEHSRFNSRTKAIMKIAIVWAISIGVSVPIPVIGLRDEEKVFVNNTTCVLNDPN FVLIGSFVAFFIPLTIMVITYCLTIYVLRRQALMLLHGHTEEPPGLSLDFLKCCKRNTAEEENSANPNQDQNARRRKKKERRPRGTMQAINNERKASKVLGIVFFVFLIMWCPFFITNILSVLCEKSCNQKLMEKLLNVFVW IGYVCSGINPLVYTLFNKIYRRAFSNYLRCNYKVEKKPPVRQIPRVAATALSGRELNVNIYRHTNEPVIEK **ASDNEPGIEMQVENLELPVNPSSVVSERISSV** 

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Non-Endogenous, Constitutively Activated human Serotonin Receptors and Small Molecule Modulators Thereof

Inventor(s): Behan et al.

Attorney: Gwilym John Owen Attwell

Attorney Phone No.: 215 568-3100

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FIG. 4A

**ATGGTGAACCTGAGGAATGCGGTGCATTCATTCCTTGTGCACCTAATTGGCCTATTGGTTTGGC AATGTGATATTTCTGTGAGCCCAGTAGCAGCTATAGTAACTGACATTTTCAATACCTCCGATG** GTGGACGCTTCAAATTCCCAGACGGGGTACAAAACTGGCCAGCACTTTCAATCGTCATCATAA TAATCATGACAATAGGTGGCAACATCCTTGTGATCATGGCAGTAAGCATGGAAAAGAAACTG CACAATGCCACCAATTACTTCTTAATGTCCCTAGCCATTGCTGATATGCTAGTGGGACTACTTG TCATGCCCCTGTCTCCTCGGCAATCCTTTATGATTATGTCTGGCCACTACCTAGATATTTGTG CCCCGTCTGGATTTCTTTAGATGTTTTATTTTCAACAGCGTCCATCATGCACCTCTGCGCTATAT CGCTGGATCGGTATGTAGCAATACGTAATCCTATTGAGCATAGCCGTTTCAATTCGCGGACTA AGGCCATCATGAAGATTGCTATTGTTTGGGCAATTTCTATAGGTGTATCAGTTCCTATCCCTGT CAAATTTCGTTCTTATTGGGTCCTTCGTAGCTTTCTTCATACCGCTGACGATTATGGTGATTAC GTATTGCCTGACCATCTACGTTCTGCGCCGACAAGCTTTGATGTTACTGCACGGCCACACCGA GGAACCGCCTGGACTAAGTCTGGATTTCCTGAAGTGCTGCAAGAGGAATACGGCCGAGGAAG TCCTAGGGGCACCATGCAGGCTATCAACAATGAAAGAAAAGCTTCGAAAGTCCTTGGGATTG AGAAGTCCTGTAACCAAAAGCTCATGGAAAAGCTTCTGAATGTTGTTTTGGATTGGCTAG TTTGTTCAGGAATCAATCCTCTGGTGTATACTCTGTTCAACAAAATTTACCGAAGGGCATTCTC CAACTATTTGCGTTGCAATTATAAGGTAGAGAAAAAGCCTCCTGTCAGGCAGATTCCAAGAGT TGCCGCCACTGCTTTGTCTGGGAGGGAGCTTAATGTTAACATTTATCGGCATACCAATGAACC GGTGATCGAGAAAGCCAGTGACAATGAGCCCGGTATAGAGATGCAAGTTGAGAATTTAGAGT **TACCAGTAAATCCCTCCAGTGTGGTTAGCGAAAGGATTAGCAGTGTGŤGÃ** 

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Non-Endogenous, Constitutively Activated human Seroton in Receptors andSmall Molecule Modulators Thereof

Inventor(s): Behan et al

Attorney: Gwilym John Owen Attwell Attorney Phone No.: 215 568-3100

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FIG. 5A

**ATGGTGAACCTGAGGAATGCGGTGCATTCATTCCTTGTGCACCTAATTGGCCTATTGGTTTGGCAAT GTGATATTTCTGTGAGCCCAGTAGCAGCTATAGTAACTGACATTTTCAATACCTCCGATGGTGGACG** CTTCAAATTCCCAGACGGGGTACAAAACTGGCCAGCACTTTCAATCGTCATCATAATAATCATGAC <u>AATAGGTCGCAACATCCTTGTGATCATGGCAGTAAGCATGGAAAAGAAACTGCACAATGCCACCA</u> **ATTACTTCTTAATGTCCCTAGCCATTGCTGATATGCTAGTGGGACTACTTGTCATGCCCCTGTCTCTC** CTGGCAATCCTTTATGATTATGTCTGGCCATCAACTAGATATTTGTGCCCGTCTGGATTTCTTTAGA TGTTTTATTTTCAACAGCGTCCATCATGCACCTCTGCGCTATATCGCTGGATCGGTATGTAGCAATA CGTAATTCTATTGAGCATAGCCGTTTCAATTCGCGGACTAAGGCCATCATGAAGATTGCTATTGTTT GGGCAATTTCTATAGGTGTATCAGTTCCTATCCCTGTGATTGGACTGAGGGACGAAGAAAAGGTGT TCGTGAACAACACGACGTGCGTGCTCAACGACCCAAATTTGCTTCTTATTGGGTCCTTCGTAGCTTT CTTCATACCGCTGACGATTATGGTGATTACGTATTGCCTGACCATCTACGTTCTGCGCCGACAAGCT TTGATGTTACTGCACGGCCACACCGAGGAACCGCCTGGACTAAGTCTGTATTTCCTGAACTGCTGC GAAAGTCCTTGGGATTGTTTTCTTTTGTGTTTCTGATCATGTGGTGCCCATTTTTCATTACCAATATTC GATTGGCTATGTTTGTTCAGGATTCAATCCTCTGGTGTATACTCTGTTCAACAAAATTTACCGAAGG GCATTCTCCAACTATTTGCGTTGCAATTATAAGGTAGAGAAAAAGCCCTCCTGTCAGGCAGATTCCA **AGAGTTGCCGCCACTGCTTTGTCTGGGAGGGAGCTTATTGTTAACATTTATCGGCATACCAATGAA** CCGGTGATCGAGAAAGCCAGTGACAATGAGCCCGGTATAGAGATGCAAGTTGAGAATTTAGAGTT ACCAGTAAATCCCTCCAGTGTGGTTAGCGAAAGGATTAGCAGTGTGTGA

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Non-Endogenous, Constitutively Activated human Serotonin Receptors and

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Attorney: Gwilym John Owen Attwell

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Attorney Phone No.: 215 568-3100

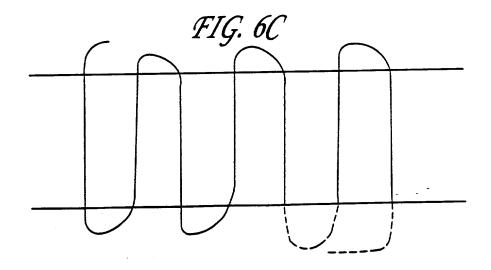
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FIG. 5B

MVNLRNAVHSFLVHLIGLLVWQCDISVSPVAAIVTDIFNTSDGGRFKFPDGVQNWPALSIVIIIIMTI **GGNILVIMAVSMEKKLHNATNYFLMSLAIADMLVGLLVMPLSLLAILYDYVWPLPRYLCPVWISL** DVLFSTASIMHLCAISLDRYVAIRNPIEHSRFNSRTKAIMKIAIVWAISIGVSVPIPVIGLRDEEKVFV NNTTCVLNDPNFVLIGSFVAFFIPLTIMVITYCLTTYVLRRQALMLLHGHTEEPPGLSDFLKCCKRN TAEEENSANPNQDQNARRRKKKERRPRGTMQAINNERKAKKVLGIVFFVFLIMWCPFFITNILSVL CEKSCNQKLMEKLLNVFVWIGYVCSGINPLVYTLFNKIYRRAFSNYLRCNYKVEKKPPVRQIPRV **AATALSGRENLNVNIYRHTNEPVIEKASDNEPGIEMQVENLELPVNPSSVVSERISSV** 

FIG. 6B

MDILCEENTSLSSTTNSLMQLNDDNRLYSNDFNSGEANTSDAFNWTVDSENRTNLSCEGCLSPSCL SLLHLQEKNWSALLTAVVIILLTIAGNILVIMAVSLEKKLQNATNYFLMSLAIADMLLGFLVMPVSM LTILYGYRWPLPSKLCAVWIYLDVLFSTASIMHLCAISLDRYVAIQNPIHHSRFNSRTKAFLKIIAVW TISVGISMPIPVFGLQDDSKVFKEGSCLLADDNFVLIGSFVSFFIPLTIMVITYFLTIKVLRRQALMLL HGHTEEPPGLSLDFLKCCKRNTAEEENSANPNQDQNARRRKKKERRPRGTMQAINNERKAS KVLGIVFFLFVVMWCPFFITNIMAVICKESCNEDVIGALLNVFVWIGYLSSAVNPLVYTLFNKIYR RAFSNYLRCNYKVEKKPPVRQIPRVAATALSGRELNVNIYRHTNEPVIEKASDNEPGIEMQVE NLELPVNPSSVVSERISSV



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Non-Endogenous, Constitutively Activated human Serotonin Receptors and Small Molecule Modulators Thereof

Inventor(s): Behan et al.

Attorney: Gwilym John Owen Attwell Attorney Phone No.: 215 568-3100

FIG. 6A

ATGGATATTCTTTGTGAAGAAAATACTTCTTTGAGCTCAACTACGAACTCCCTAATGCAATTA <u>AATGATGACAACAGGCTCTACAGTAATGACTTTAACTCCGGAGAAGCTAACACTTCTGATGCA</u> TTTAACTGGACAGTCGACTCTGAAAATCGAACCAACCTTTCCTGTGAAGGGTGCCTCTCACCG TCGTGTCTCTCCTTACTTCATCTCAGGAAAAAAACTGGTCTGCTTTACTGACAGCCGTAGTGA TTATTCTAACTATTGCTGGAAACATACTCGTCATCATGGCAGTGTCCCTAGAGAAAAAGCTGC AGAATGCCACCAACTATTTCCTGATGTCACTTGCCATAGCTGATATGCTGCTGGGTTTCCTTGT CATGCCCGTGTCCATGTTAACCATCCTGTATGGGTACCGGTGGCCTCTGCCGAGCAAGCTTTGT GCAGTCTGGATTTACCTGGACGTGCTCTTCTCCACGGCCTCCATCATGCACCTCTGCGCCATCT CGCTGGACCGCTACGTCGCCATCCAGAATCCCATCCACCACAGCCGCTTCAACTCCAGAACTA AGGC ATTTCTG AAAATCATTGCTGTTTGGACCATATCAGTAGGTATATCCATGCCAATACCAG **TCTTTGGGCTACAGGACGATTCGAAGGTCTTTAAGGAGGGGAGTTGCTTACTCGCCGATGATA ACTITIGATE GATE GATE TITTE TO TO ATTITITE ATTICCT TAACCATCAT GATGATCACCTAC** TTTCTAACTATCAAGGTTCTGCGCCCGACAAGCTTTGATGTTACTGCACGGCCACACCGAG GAACCGCCTGGACTAAGTCTGGATTTCCTGAAGTGCTGCAAGAGGAATACGGCCGAGGA AGACGTCCTAGGGGCACCATGCAGGCTATCAACAATGAAAAGAAAAGCTTCGAAGGTACT GGGCATCGTCTTCTTCTGTTTGTGGTGATGTGGTGCCCTTTCTTCATCACAAACATCATGGCC GTCATCTGCAAAGAGTCCTGCAATGAGGATGTCATTGGGGCCCTGCTCAATGTGTTTGGTTTGG ATCGGTTATCTCTTCAGCAGTCAACCCACTAGTCTATACTCTGTTCAACAAAATTTACCGA AGGGCATTCTCCAACTATTTGCGTTGCAATTATAAGGTAGAGAAAAAGCCTCCTGTCAG ATCGGCATACCAATGAACCGGTGATCGAGAAAGCCAGTGACAATGAGCCCGGTATAGAG **ATGCAAGTTGAGAATTTAGAGTTACAGTAAATCCCTCCAGTGTGGTTAGCGAAAGGAT** TAGCAGTGTGTGA

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Inventor(s): Behan et al.

Attorney: Gwilym John Owen Attwell

Attorney Phone No.: 215 568-3100

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FIG. 7A

**ATGGATATTCTTTGTGAAGAAAATACTTCTTTGAGCTCAACTACGAACTCCCTAATGCAATTA** <u>AATGATGACAACAGGCTCTACAGTAATGACTTTAACTCCGGAGAAGCTAACACTTCTGATGCA</u> TTTAACTGGACAGTCGACTCTGAAAATCGAACCAACCTTTCCTGTGAAGGGTGCCTCTCACCG TCGTGTCTCTCCTTACTTCATCTCCAGGAAAAAAACTGGTCTGCTTTACTGACAGCCGTAGTGA TTATTCTAACTATTGCTGGAAACATACTCGTCATCATGGCAGTGTCCCTAGAGAAAAAGCTGC AGAATGCCACCAACTATTTCCTGATGTCACTTGCCATAGCTGATATGCTGCTGGGTTTCCTTGT CATGCCCGTGTCCATGTTAACCATCCTGTATGGGTACCGGTGGCCTCTGCCGAGCAAGCTTTGT GCAGTCTGGATTTACCTGGACGTGCTCTTCTCCACGGCCTCCATCATGCACCTCTGCGCCATCT CGCTGGACCGCTACGTCGCCATCCAGAATCCCATCCACCACAGCCGCTTCAACTCCAGAACTA <u>AGGCATTTCTGAAAATCATTGCTGTTTGGACCATATCAGTAGGTATATCCATGCCAATACCAG</u> TCTTTGGGCTACAGGACGATTCGAAGGTCTTTAAGGAGGGGAGTTGCTTACTCGCCGATGATA <u>ACTITICTCCTGATCGGCTCTTTTGTGTCATTTTTCATTCCCCTGACGATTATGGTGATTACGT</u> <u>ATTGCCTGACCATCTACGTTCTGCGCCGACAAGCTTTGATGTTACTGCACGGCCACACC</u> **GAGGAACCGCCTGGACTAAGTCTGGATTTCCTGAAGTGCTGCAAGAGGAATACGGCCGA** <u>CCTTGGGATTGTTTTCTTTGTGTTTCTGATC</u>ATGTGGTGCCCTTTCTTCATCACAAACATCA TGGCCGTCATCTGCAAAGAGTCCTGCAATGAGGATGTCATTGGGGCCCTGCTCAATGTGTTTG TTTGGATCGGTTATCTCTCTCAGCAGTCAACCCACTAGTCTA<u>TACTCTGTTCAACAAAATTT</u> <u>ACCGAAGGGCATTCTCCAACTATTTGCGTTGCAATTATAAGGTAGAGAAAAAGCCTCCT</u> <u>CATTTATCGGCATACCAATGAACCGGTGATCGAGAAAGCCAGTGACAATGAGCCCGGTA</u> <u>TAGAGATGCAAGTTGAGAATTTAGAGTTACCAGTAAATCCCTCCAGTGTGGTTAGCGAA</u> <u>AGGATTAGCAGTGTGTGA</u>

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Small Molecule Modulators Thereof

Inventor(s): Behan et al.

Attorney: Gwilym John Owen Attwell

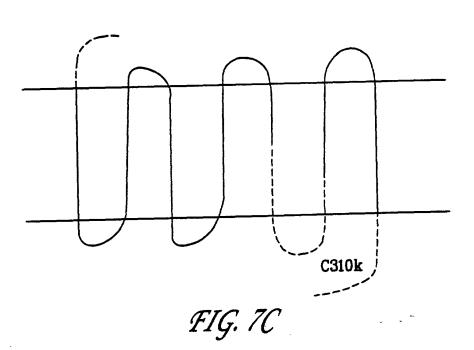
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 $Non-Endogenous, Constitutively\ Activated\ human\ Seroton in\ Receptors\ and$ 

FIG. 7B

MDILCEENTSLSSTTNSLMQLNDDNRLYSNDFNSGEANTSDAFNWTVDSENRTNLSCEGCLSPSCL
SILHIQEKNWSALLTAVVIILTIAGNILVIMAVSLEKKLQNATNYFLMSLAIADMILGFLVMPVSM
LTILYGYRWPLPSKLCAVWIYLDVLFSTASIMHLCAISLDRYVAIQNPIHHRSFNSRTKAFLKIIAVW
TISVGISMPIPVFGLQDDSKVFKEGSCILADDNFVLIGSFVSFFIPLTIMVTTYCLTTYVLRRQALML
LHGHTEEPPGLSLDFLKCCKRNTAEEENSANPNODQNARRRKKKERRPRGTMQAINNERKA
KKVLGIVFFYFLDMWCPFFTTNIMAVICKESCNEDVIGALLNVFVWIGYLSSAVNPLVYTLFNKIY
RRAFSNYLRCNYKVEKKPPVRQIPRVAATALSGRELNVNIYRHTNEPVIEKASDNEPGIEMQV
ENLELPVNPSSVVSERISSY



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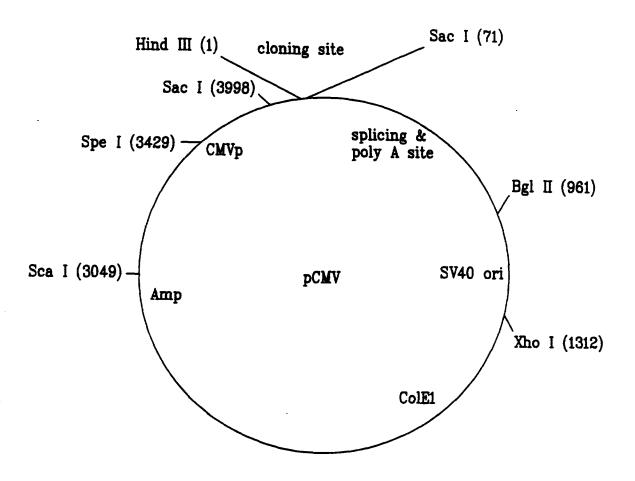
Small Molecule Modulators Thereof

Inventor(s): Behan et al.

Attorney: Gwilym John Owen Attwell

Attorney Phone No.: 215 568-3100

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\*Xho I (1312) to Sca I (3049) is identical to pRc/RSV Xho I (3045) to 4782.

\*Sca I (3049) to 4070 is identical to pCDM7 Amp Scal (2524) to 3545.

\*multiple cloning site includes Hind III to Sac I of pBluescript IL

\*110 to 1312 is identical to pCMD7 Amp 76 to 1278.

\*Sac I and Spe I in MCS are not unique.

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FIG. 8

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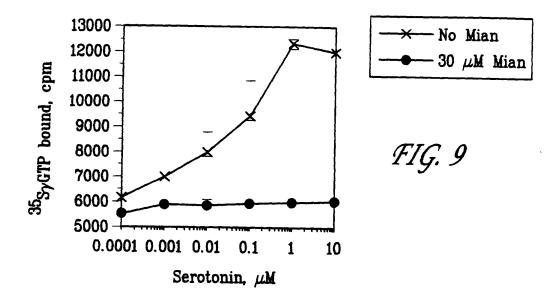
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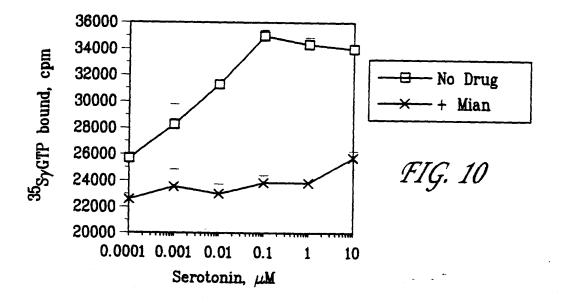
Inventor(s): Behan et al.

Attorney: Gwilym John Owen Attwell

Attorney Phone No.: 215 568-3100

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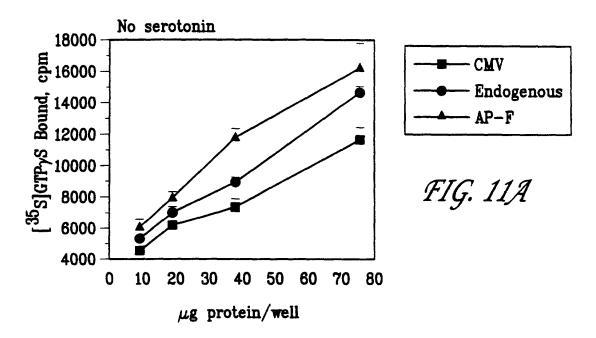
Inventor(s): Behan et al.

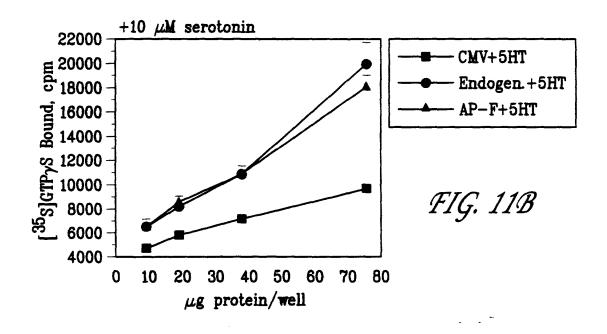
Attorney: Gwilym John Owen Attwell

Attorney Phone No.: 215 568-3100

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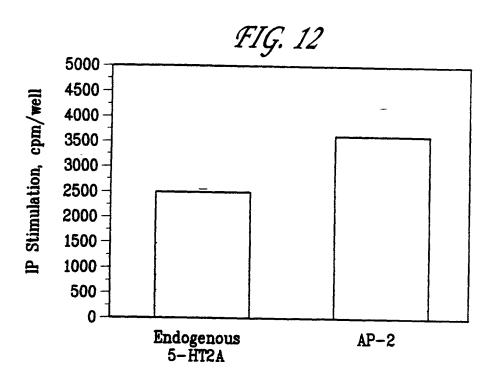
Small Molecule Modulators Thereof

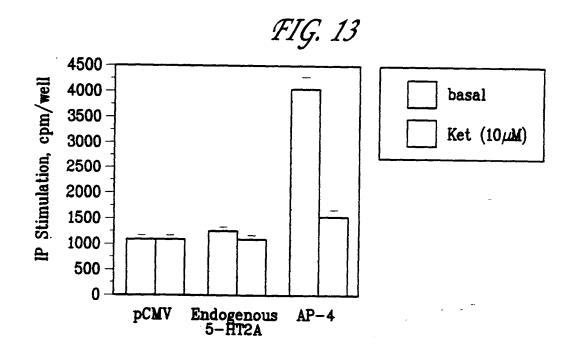
Inventor(s): Behan et al.

Attorney: Gwilym John Owen Attwell

Attorney Phone No.: 215 568-3100

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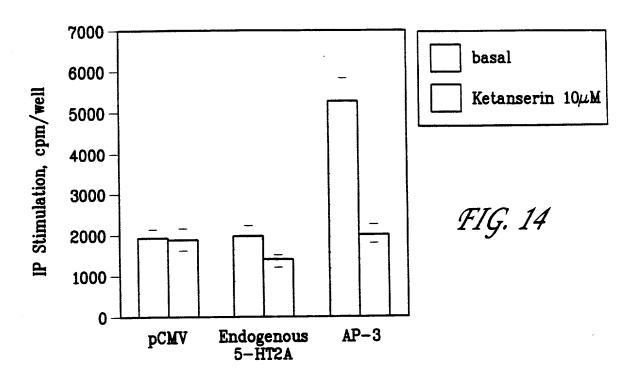
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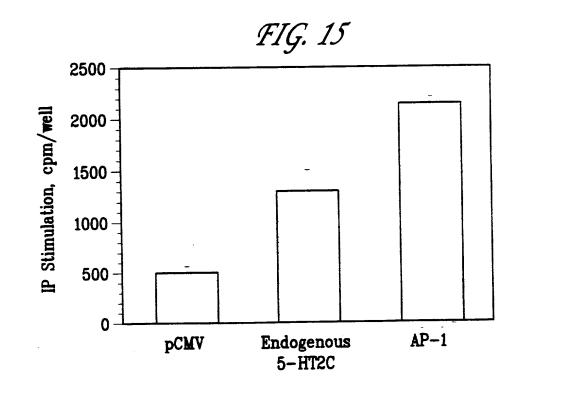
Inventor(s): Behan et al.

Attorney: Gwilym John Owen Attwell

Attorney Phone No.: 215 568-3100

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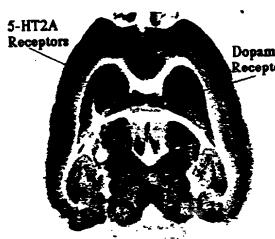
Small Molecule Modulators Thereof

Inventor(s): Behan et al.

Attorney: Gwilym John Owen Attwell

Attorney Phone No.: 215 568-3100

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Dopamine D2 Receptors

FIG. 16A



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FIG. 16B



FIG. 16C

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